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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/557,583	03/03/2006	Bonabes O. De Rouge	50538/016001	3863

21559 7590 03/24/2009  
CLARK & ELBING LLP  
101 FEDERAL STREET  
BOSTON, MA 02110

EXAMINER
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RUSSEL, JEFFREY E

ART UNIT	PAPER NUMBER
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1654

NOTIFICATION DATE	DELIVERY MODE
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03/24/2009

ELECTRONIC

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentadministrator@clarkelbing.com

<b>Office Action Summary</b>	<b>Application No.</b> 10/557,583	<b>Applicant(s)</b> DE ROUGE ET AL.	
	<b>Examiner</b> Jeffrey E. Russel	<b>Art Unit</b> 1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 07 July 2008.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-18 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-10 and 14-18 is/are rejected.
- 7) ☒ Claim(s) 11-13 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)          | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

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1. Applicant's election with traverse of the species GPG and the terminator  $\omega$ -amino fatty acid in the reply filed on July 7, 2008 is acknowledged. The elected species has been examined and determined to be novel and unobvious over the prior art of record or any combination thereof. Accordingly, the election of species requirement/holding of lack of unity set forth in the Office action mailed June 4, 2008 is withdrawn. Search and examination has been extended throughout the full scope of the instant claimed invention.

2. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the following reasons:

The Sequence Listing filed November 14, 2007 was not accompanied by a statement of no new matter, as is required by 37 CFR 1.821(g) and/or 1.825(a).

Correction is required.

The Sequence Listing filed November 14, 2007 was approved by STIC for matters of form.

3. The substitute specification filed November 16, 2005 has been entered.

The amendment to the specification filed November 14, 2007 has not been entered because the amendment instructions do not unambiguously identify the locations of the paragraphs to be amended, as required by 37 CFR 1.121(b)(1)(i). It appears that the amendment instructions refer to the specification as filed in the PCT application rather than the substitute specification filed November 16, 2005.

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4. The disclosure is objected to because of the following informalities: SEQ ID NOS must be inserted after those amino acid sequences subject to the sequence disclosure rules. See 37 CFR 1.821(d). Such sequences are present at, e.g., pages 2-5, 11, 12, and 19 of the specification. (If the proposed specification amendment filed November 14, 2007 was to be re-submitted with updated amendment instructions, this objection would be overcome.) Appropriate correction is required.

5. Claim 14 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The meaning of the term "TAT-derived peptide" in claim 14 is unclear. It is not clear if this is a proper noun, i.e. designating a single peptide having a single amino acid sequence. Alternatively, it is not clear what degree of structural and/or functional similarity a peptide must share with TAT in order to constitute a TAT-derived peptide and therefore embraced within the scope of the claim. The term is not defined in the specification. The use of the trademark "penetratin®" in claim 14 is indefinite. A trademark, by definition, indicates a source of goods, rather than the goods themselves. To the extent that Applicants are relying upon the trademark to identify a particular chemical compound, the use of the trademark is therefore indefinite. To the extent that Applicants do not intend for the trademark, i.e. the source of the product, to constitute a claim limitation, the use of the trademark would also be indefinite. See MPEP 2173.05(u). The meaning of the term "Kpam" in claim 14 is unknown. The term is not defined in Applicants' specification, nor is the term commonly used in chemical arts to define a particular chemical compound.

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6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

For the purposes of this invention, the level of ordinary skill in the art is deemed to be at least that level of skill demonstrated by the patents in the relevant art. *Joy Technologies Inc. v. Quigg*, 14 USPQ2d 1432 (DC DC 1990). One of ordinary skill in the art is held accountable not only for specific teachings of references, but also for inferences which those skilled in the art may reasonably be expected to draw. *In re Hoeschele*, 160 USPQ 809, 811 (CCPA 1969). In addition, one of ordinary skill in the art is motivated by economics to depart from the prior art to reduce costs consistent with desired product properties. *In re Clinton*, 188 USPQ 365, 367 (CCPA 1976); *In re Thompson*, 192 USPQ 275, 277 (CCPA 1976).

7. Claims 1-3, 8, 9, and 14 are rejected under 35 U.S.C. 102(b) as being anticipated by the WO Patent Application 98/14587. The WO Patent Application '587 teaches the peptide

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GPGRAPH linked to a polylysine, which can be linked to a TAT peptide. Preferably eight copies of GPGRAPH are linked to the polylysine, and the GPGRAPH-polylysine is preferably linked to the amino terminus of the TAT peptide. The compositions of the WO Patent Application '587 are used therapeutically to inhibit HIV replication, i.e. transcription or translation, in mammalian cells. See, e.g., page 5, lines 25-27; page 7, lines 3-5; page 16, lines 29-32; and page 23, line 15 - page 24, line 3. Because the compositions of the WO Patent Application '587 act to inhibit HIV replication, which is known to occur inside of cells, inherently the TAT peptide of the WO Patent Application '587 must be capable of penetrating cell membranes to the extent claimed by Applicants. Alternatively, in view of the similarity in source of the TAT peptide and in view of the similarity in structure and anti-HIV activity between the compositions of the WO Patent Application '587 and Applicants' claimed compounds, inherently the compositions of the WO Patent Application '587 will comprise a peptidic cell membrane penetrating agent. Sufficient evidence of similarity is deemed to be present between the compositions of the WO Patent Application '587 and Applicants' claimed compounds to shift the burden to Applicants to provide evidence that the claimed compounds are unobviously different than the compositions of the WO Patent Application '587.

8. Claim 7 is rejected under 35 U.S.C. 103(a) as being obvious over the WO Patent Application 98/14587. Application of the WO Patent Application '587 is the same as in the above rejection of claims 1-3, 8, 9, and 14. The WO Patent Application '587 teaches GPGRAPH linked to a multibranch structure, but does not teach a structure comprising two branches. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to determine all operable and optimal number of branches for the compositions of the WO

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Patent Application '587, because the WO Patent Application '587 is not limited to any particular number of branches, and because for conjugates involving multibranch structures, the number of branches is an art-recognized result-effective variable which is routinely determined and optimized.

9. Claims 4-6, 10, and 15-18 are rejected under 35 U.S.C. 103(a) as being obvious over the WO Patent Application 98/14587 as applied against claims 1-3, 8, 9, and 14 above, and further in view of the WO Patent Application 98/29443. The WO Patent Application '587 teaches compositions comprising a consensus sequence of the HIV-1 surface envelope glycoprotein gp120 V3 loop, GPGRAPH, and does not disclose compositions comprising RQGY sequences. The WO Patent Application '443 teaches consensus sequence peptides derived from the HIV-1 envelope transmembrane glycoprotein gp41. The peptides comprise RQGY, and preferably is RQGYSP. The WO Patent Application '443 teaches multiple copies, from 2 to 16 and preferably from 8 to 16 copies, of these peptides attached to a core matrix of polylysine, and teaches their use as anti-HIV peptides, being virostatic and preventing cell-to-cell fusion. See, e.g., the Abstract; and page 2, first full paragraph. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to substitute the RQGY peptides of the WO Patent Application '443 for the GPGRAPH peptides of the WO Patent Application '587, because both peptides are used as anti-HIV agents in the form of a branched polylysine conjugate, and because substitution of one functionally equivalent peptide for another functionally equivalent peptide in a conjugate is routine and prima facie obvious. The WO Patent Application '587 does not teach a structure comprising two branches. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to

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determine all operable and optimal number of branches for the compositions of the WO Patent Application '587 as modified above by the WO Patent Application '443, because the WO Patent Application '587 is not limited to any particular number of branches, because for conjugates involving multibranch structures, the number of branches is an art-recognized result-effective variable which is routinely determined and optimized, and because the WO Patent Application '443 teaches that as few as two branches are useful for its peptides attached to a multibranch structure.

10. Claims 11-13 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. The prior art of record does not teach or suggest a compound as is recited in claim 1 in which the terminator is (a) an  $\omega$ -amino-fatty acid having from 4 to 10 carbon atoms and from 0 to 2 carbon-carbon double bonds.

Boutillon et al (U.S. Patent No. 5,993,823) is cited as art of interest, teaching anti-HIV lipopeptides. However, except for the 10-carbon atom fatty acids, the fatty acids of Boutillon et al are larger than those claimed by Applicants. Further, Boutillon et al do not teach or suggest  $\omega$ -amino-fatty acids.

Tam (U.S. Patent No. 5,580,563) is also cited as art of interest, teaching anti-HIV peptides conjugated to fatty acids. However, Tam also does not teach or suggest  $\omega$ -amino-fatty acids.

Fischer et al (U.S. Patent No. 6,472,507) is cited as art of interest, teaching a drug system comprising a drug moiety linked to a carrier moiety such as a penetratin. However, Fischer et al exclude peptidic drugs as their drug moiety.



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11. The information disclosure statement filed October 2, 2006 fails to comply with 37 CFR 1.98(a)(1), which requires the following: (1) a list of all patents, publications, applications, or other information submitted for consideration by the Office; (2) U.S. patents and U.S. patent application publications listed in a section separately from citations of other documents; (3) the application number of the application in which the information disclosure statement is being submitted on each page of the list; (4) a column that provides a blank space next to each document to be considered, for the examiner's initials; and (5) a heading that clearly indicates that the list is an information disclosure statement. The information disclosure statement has been placed in the application file, but the information referred to therein has not been considered. See also MPEP 609.04(a)(I).

A list of the references being cited was not included with the information disclosure statement.

12. The references cited in the International Search Report (EPO Search Office, mailing date 16 December 2004) have been considered, but will not be listed on any patent resulting from this application because they were not provided on a separate list in compliance with 37 CFR 1.98(a)(1). In order to have the references printed on such resulting patent, a separate listing, preferably on a PTO/SB/08A and 08B form, must be filed within the set period for reply to this Office action. See also MPEP 609.03.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey E. Russel at telephone number (571) 272-0969. The examiner can normally be reached on Monday-Thursday from 8:00 A.M. to 5:30 P.M. The examiner can also be reached on alternate Fridays.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Cecilia Tsang can be reached at (571) 272-0562. The fax number for formal communications to be entered into the record is (571) 273-8300; for informal communications such as proposed amendments, the fax number (571) 273-0969 can be used. The telephone number for the Technology Center 1600 receptionist is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Jeffrey E. Russel/  
Primary Examiner, Art Unit 1654

JRussel  
March 20, 2009